



General

Guideline Title

A.S.P.E.N. clinical guidelines: nutrition support of neonatal patients at risk for metabolic bone disease.

Bibliographic Source(s)

Nehra D, Carlson SJ, Fallon EM, Kalish B, Potemkin AK, Gura KM, Simpser E, Compher C, Puder M, American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. clinical guidelines: nutrition support of neonatal patients at risk for metabolic bone disease. JPEN J Parenter Enteral Nutr. 2013 Sep;37(5):570-98. [72 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions for the grading of recommendations (Strong, Weak, Further research needed) and quality of evidence (High, Moderate, Low, Very Low) are provided at the end of the "Major Recommendations" field.

What Maternal Risk Factors Predispose the Neonate to Metabolic Bone Disease?

Maternal vitamin D deficiency is a risk factor for neonatal vitamin D deficiency and abnormal bone health, and the authors suggest that pregnant women be screened for vitamin D deficiency and those that are deficient be supplemented (Weak). Insufficient data are available to determine the effect of maternal magnesium sulfate and folic acid use on neonatal bone health (Further research needed).

Evidence Grade: Low

What Is the Optimal Type of Feeding to Promote Neonatal Bone Health?

When available, the authors suggest human milk with nutrient fortifier for the preterm infant (Weak). When human milk is not available, the authors suggest that nutrient-enriched formula be used (Weak).

Evidence Grade: Low

When and How Should Vitamin D Supplements Be Administered?

The authors suggest vitamin D supplementation for healthy breastfed infants and those with malnutrition and/or rickets (Weak). Further studies are needed to determine the optimal dose, route, and duration of supplementation in each of these conditions (Further research needed).

Evidence Grade: Low

Does Parenteral Nutrition (PN) Predispose a Neonate to Metabolic Bone Disease, and if So, Are There PN Formulation Recommendations to Minimize This Risk?

The authors suggest that PN predisposes the infant to metabolic bone disease (Weak). The authors suggest using PN formulations with high-dose calcium and phosphorus content (Weak). PN aluminum is a risk factor for metabolic bone disease of the neonate (Strong), and the authors suggest that future efforts be made to reduce the aluminum content of PN.

Evidence Grade: Low/Moderate

Definitions:

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology is outlined in the A.S.P.E.N. guideline "Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines" (see the "Availability of Companion Documents" field).

Quality of Evidence

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Strength of Recommendation

Strong	Net benefits outweigh harms
Weak	Tradeoffs for patient are important
Further Research Needed	Uncertain tradeoffs

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Metabolic bone disease, with resulting delayed bone growth, osteopenia, and rickets

Guideline Category

Evaluation

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Nutrition

Obstetrics and Gynecology

Pediatrics

Intended Users

Advanced Practice Nurses

Dietitians

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To identify maternal and neonatal factors that place infants at risk for metabolic bone disease and provide a rationale for nutrition strategies to prevent and treat the condition

Target Population

- Pregnant women
- Neonates and infants, including preterm neonates, who are at increased risk for metabolic bone disease

Interventions and Practices Considered

1. Screening pregnant women for vitamin D deficiency and providing supplementation when deficient
2. Use of human milk with nutrient fortifier for the preterm infant
3. Use of nutrient-enriched formula when human milk is not available
4. Vitamin D supplementation for healthy breastfed infants and those with malnutrition and/or rickets
5. Use of parenteral nutrition (PN) formulations with high-dose calcium and phosphorus content
6. Reducing aluminum content of PN formulas

Major Outcomes Considered

- Biochemical measures: maternal and neonatal serum levels of 25-hydroxyvitamin D, parathyroid hormone, ionized calcium, phosphate, alkaline phosphatase, magnesium
- Neonatal, infant, and child bone variables (bone mineral density, bone mineral content, cross-sectional area)
- Fetal anthropometric measures
- Anthropometrics at birth and discharge
- Radiographic bone abnormalities
- Maternal adverse effects
- Neonatal adverse effects (birth weight, Apgar scores, magnesium and calcium levels, nursery stay, hypotonia, morbidity, mortality)

- Osteoblastic and osteoclastic bone activity
- Clinical signs of rickets

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

For the current Clinical Guideline, a PubMed search was performed to identify pertinent studies using the search terms bone AND neonate* OR infant*. The search was further focused by identifying studies containing at least 1 of the following additional key terms: aluminum; breastfed; breast fed; breast-fed; breast milk; calcium; copper; cysteine; diet; feeding; formula; human milk; magnesium; maternal; mineral; nutrition; parenteral nutrition; phosphorus; preterm formula; rickets; risk factor; total parenteral nutrition; trace element; vitamin D or vitamin K. Studies were excluded if they contained one or more of the following key terms: bone marrow transplant; bone marrow transplantation; cancer; dialysis; hyperparathyroidism; hypoparathyroidism; osteopetrorickets; renal failure; renal tubular acidosis or transplant, which allowed for the exclusion of studies addressing bone disease in the setting of these other medical conditions that were not consistent with the aims of the current Clinical Guidelines. In addition, the following limits regarding the type of study were used: humans; clinical trial; randomized controlled trial (RCT); clinical trial: phase I, phase II, phase III, phase IV; comparative study; controlled clinical trial; guideline; journal article; multicenter study; English language; and published within the last 10 years. The search was conducted on July 22, 2011.

Number of Source Documents

A total of 941 abstracts were reviewed, of which 29 papers met the inclusion criteria of the Clinical Guidelines and were included.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology is outlined in the A.S.P.E.N. guideline "Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines" (see the "Availability of Companion Documents" field).

Quality of Evidence

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Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

A systematic review of the best available evidence to answer a series of questions regarding neonatal patients at risk of metabolic bone disease receiving parenteral or enteral nutrition was undertaken and evaluated using concepts adopted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These Clinical Guidelines were developed under the guidance of the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors.

A.S.P.E.N. Clinical Guidelines has adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. Briefly, specific clinical questions where nutrition support is a relevant mode of therapy are developed and key clinical outcomes are identified. A rigorous search of the published literature is conducted, each included study is assessed for research quality, tables of findings are developed, the body of evidence for the question is evaluated, and a recommendation for clinical practice that is based on both the best available evidence and the risks and benefits to patients is developed by consensus. Recommendations are graded as strong when the evidence is strong and/or net benefits outweigh harms. Weak recommendations may be based on weaker evidence and/or important tradeoffs to the patient. When limited research is available to answer a question, no recommendation can be made.

Rating Scheme for the Strength of the Recommendations

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology is outlined in the A.S.P.E.N. guideline "Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines" (see the "Availability of Companion Documents" field).

Strength of Recommendation

Strong	Net benefits outweigh harms
Weak	Tradeoffs for patient are important
Further Research Needed	Uncertain tradeoffs

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

A consensus process was used to develop the clinical guideline recommendations prior to external and internal review and approval by the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors on March 20, 2013.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence identified and graded for each recommendation (see the "Major Recommendations" field).

The recommendations were based primarily on a comprehensive review of published reports that included randomized clinical trials and controlled and uncontrolled case series. In cases where the data did not appear conclusive, recommendations were based on the consensus opinion of the group in a process that considered the risks versus benefits.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate nutrition support of neonatal patients at risk for metabolic bone disease

Potential Harms

Aluminum is a contaminant of parenteral nutrition (PN) components, and high doses of aluminum have been shown to negatively affect both cognitive development and short-term bone health. In animals and adult humans, excess aluminum has been shown to accumulate at mineralization fronts and is associated with reduced bone formation. In addition, one study reported that bone aluminum concentrations were 10-fold higher in preterm infants who received PN for >3 weeks as compared with control subjects. It has been recently demonstrated that the currently available PN products in the United States have an aluminum content that makes it impossible to meet the new Food and Drug Administration rule of <5 mcg/kg per day of aluminum exposure in patients <50 kg. Thus, it is imperative that manufacturers develop new methods to reduce the aluminum contamination in their products and healthcare professionals be aware of the aluminum exposure in PN-dependent neonates.

Qualifying Statements

Qualifying Statements

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines are based upon general conclusions of health professionals who, in developing such guidelines, have balanced potential benefits to be derived from a particular mode of medical therapy against certain risks inherent with such therapy. However, the professional judgment of the attending health professional is the primary component of quality medical care. Because guidelines cannot account for every variation in circumstances, the practitioner must always exercise professional judgment in their application. These Clinical Guidelines are intended to supplement, but not replace, professional training and judgment.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Core Need

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Sep

Guideline Developer(s)

American Society for Parenteral and Enteral Nutrition - Professional Association

Source(s) of Funding

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Guideline Committee

Not stated

Composition of Group That Authored the Guideline

Authors: Deepika Nehra, MD; Sarah J. Carlson, MD; Erica M. Fallon, MD; Brian Kalish, BS; Alexis K. Potemkin, RN, BSN; Kathleen M. Gura, PharmD, BCNSP; Edwin Simpson, MD; Charlene Compher, PhD, RD, CNSC, LDN, FADA; Mark Puder, MD, PhD; American Society for Parenteral and Enteral Nutrition

Financial Disclosures/Conflicts of Interest

None declared

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [Journal of Parenteral and Enteral Nutrition Web site](#) .

Availability of Companion Documents

The following is available:

- Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines. American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.); 2012 Jan. 5 p. Electronic copies: Available from the [Journal of Parenteral and Enteral Nutrition Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 20, 2013. The information was verified by the guideline developer on January 6, 2014.

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